Complete Summary

GUIDELINE TITLE

Guideline for the use of imaging in the management of myeloma.

BIBLIOGRAPHIC SOURCE(S)

D'Sa S, Abildgaard N, Tighe J, Shaw P, Hall-Craggs M. Guidelines for the use of imaging in the management of myeloma. Br J Haematol 2007 Apr;137(1):49-63. [115 references] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Myeloma

GUIDELINE CATEGORY

Diagnosis
Management
Technology Assessment

CLINICAL SPECIALTY

Hematology
Nuclear Medicine

Oncology
Radiology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To set out the key areas of strategy in the effective use of imaging in the management of myeloma

TARGET POPULATION

Patients with multiple myeloma and associated diseases

INTERVENTIONS AND PRACTICES CONSIDERED

Diagnostic Imaging

1. Skeletal survey using plain radiography (x-ray)
2. Magnetic resonance (MR) imaging
3. Computed tomography (CT)
4. Bone scintigraphy (not recommended for routine staging of myeloma)
5. Dual energy x-ray absorptiometry (DEXA) scanning (not recommended)
6. Positron emission tomography (PET)
7. ^{99}Technetium sestamibi (MIBI) scanning
8. Serum amyloid P component scintigraphy

Management

1. Use of imaging in the management of vertebral collapse
2. Use of imaging in the assessment of response to therapy and disease relapse (not recommended routinely)

MAJOR OUTCOMES CONSIDERED

- Sensitivity and specificity of imaging technique
- Quantification of disease burden

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Review of key literature including Cochrane database, Medline and Internet searches updated to 28 February 2006.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Ia Evidence obtained from meta-analysis of randomised controlled trials

Ib Evidence obtained from at least one randomised controlled trial

IIa Evidence obtained from at least one well-designed, non-randomised study, including phase II trials and case-control studies

IIb Evidence obtained from at least one other type of well-designed, quasi-experimental study (i.e. studies without planned intervention including observational studies)

III Evidence obtained from well-designed, non-experimental descriptive studies. Evidence obtained from meta-analysis or randomised controlled trials or phase II studies which is published only in abstract form

IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses
Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

- Consultation with representatives of other specialties, including surgeons and specialists in nuclear medicine.

- Recommendations made based on the literature review and consensus of expert opinion.
- Completion date 31st March 2006.
- Adherence to the British Committee for Standards in Haematology (BCSH) procedure for guidelines development (http://www.bcshguidelines.com/process1.asp).

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Grades of Recommendations

Grade A, Evidence levels Ia and Ib Recommendation based on at least one randomised controlled trial of good quality and consistency addressing specific recommendation

Grade B, Evidence levels IIa, IIb, and III Recommendation based on well-conducted studies but no randomised controlled trials on the topic of recommendation

Grade C, Evidence level IV Evidence from expert committee reports and/or clinical experiences of respected authorities

COST ANALYSIS

Published cost analyses were reviewed.

- The important consideration is whether the increased costs involved and/or greater exposure to radiation is justifiable in terms of improved clinical outcome.
- Although impressive 3-dimensional images are available on completion of positron emission tomography/computed tomography investigation, this occurs at the expense of greater cost and radiation exposure.

METHOD OF GUIDELINE VALIDATION

Not stated

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Recommendation grades (**A-C**) and levels of evidence (**Ia-IV**) are defined at the end of the "Major Recommendations" field.

Minimising Radiation Exposure

- Robust systems should be in place for timely reporting and secure storage of X-ray films in order to avoid repeating investigations that have already been done.
- Accurate clinical information should be provided to the Radiology Department when the imaging request is made to ensure that the right imaging technique is performed at the right time, specifying whether the request pertains to a diagnostic work up or investigation of new symptoms in a patient who is known to have myeloma, including details of prior therapy.

Use of Imaging at Diagnosis

Skeletal Survey

- As part of the staging procedure of newly diagnosed myeloma, the skeletal survey should include a posteroanterior (PA) view of the chest, antero-posterior (AP) and lateral views of the cervical spine (including an open mouth view), thoracic spine, lumbar spine, humeri and femora, AP and lateral views of the skull and AP view of the pelvis. In addition, any symptomatic areas should be specifically visualised with appropriate views (**Grade C recommendation; level IV evidence**).

Magnetic Resonance (MR) Imaging

- Urgent MR imaging is the diagnostic procedure of choice to assess suspected cord compression in myeloma patients even in the absence of vertebral collapse (**Grade B recommendation; level IIB evidence**).
- MR imaging of the whole spine should be performed in addition to the skeletal survey as part of staging in all patients with an apparently solitary plasmacytoma of bone irrespective of site of index lesion (**Grade B recommendation; level IIB evidence**).
- MR imaging should be used to clarify the significance of ambiguous computed tomography (CT) findings, as these two imaging techniques can give complementary information (**Grade C recommendation; level IV evidence**).

Computed Tomography

- Urgent CT may be used to establish the presence of suspected cord compression in cases where MR imaging is unavailable, impossible due to patient intolerance or contraindicated (e.g. intraorbital metallic foreign bodies or cardiac pacemakers) (**Grade B recommendation; level III evidence**).
- CT of the spine may be considered to clarify the presence or absence of bone destruction in cases of clinical concern where MR is negative (**Grade B recommendation; level III evidence**).
- CT should be used to clarify the significance of ambiguous plain radiographic findings, such as equivocal lytic lesions, especially in parts of the skeleton that are difficult to visualise on plain radiographs, such as ribs, sternum and scapulae (**Grade B recommendation; level III evidence**).
- CT may identify lesions that are negative on plain radiography, and should be considered in patients who remain symptomatic despite having no evidence of osteolysis on the skeletal survey (**Grade B recommendation; level III evidence**).

- CT is indicated to delineate the nature and extent of soft tissue disease, and where appropriate, tissue biopsy may be guided by CT scanning (**Grade B recommendation; level IIB evidence**).

Bone Scintigraphy

- Bone scintigraphy has no place in the routine staging of myeloma.

Dual Energy X-Ray Absorptiometry (DEXA) Scanning

- Routine assessment of bone mineral density cannot be recommended, owing to the methodological difficulties of the technique and the universal use of bisphosphonates in all symptomatic myeloma patients.

Positron Emission Tomography (PET) and ^{99}Technitium Sestamibi (MIBI) Scanning

- Based on currently available evidence, neither PET nor MIBI imaging can be recommended for routine use in the management of myeloma patients.
- Either technique may be useful in selected cases that warrant clarification of previous imaging findings, but such an approach should ideally be made within the context of a clinical trial (**Grade C recommendation; level IV evidence**).
- The evidence for the sensitivity of PET scanning is most convincing in the setting of extramedullary disease. It is therefore reasonable to consider PET scanning in this setting, to clarify the extent of extramedullary disease, in cases where other imaging techniques have failed to clarify the situation (**Grade B recommendation; level III evidence**).
- If the decision to perform PET scanning has been taken, it is advisable to avoid undertaking the procedure within 4 weeks of chemotherapy or 3 months of radiotherapy (**Grade B recommendation; level III evidence**).

Serum Amyloid P (SAP) Component Scintigraphy

- A diagnostic SAP scan should be requested if possible in any patient suspected of having primary (AL) amyloidosis as a complication of their plasma cell dyscrasias in addition to obtaining tissue biopsy evidence whenever possible (**Grade B recommendation; level IIB evidence**).
- Follow up SAP scans should be performed every 6 to 12 months in accordance with specialist centre policy, to assess response to therapy or to monitor a patient with confirmed amyloidosis on a watchful waiting programme (**Grade B recommendation; level IIB evidence**).

<u>Use of Imaging in the Management of Vertebral Collapse</u>

- Urgent MR imaging is the diagnostic procedure of choice to assess suspected cord compression in myeloma patients with vertebral collapse (**Grade B recommendation; level IIB evidence**).
- Patients being considered for percutaneous vertebroplasty should undergo AP and lateral views of the cervical, thoracic and lumbar spine and CT or MR

imaging of the target area to exclude spinal cord compression (**Grade C recommendation; level IV evidence**).

Assessment of Response to Therapy and Disease Relapse

Skeletal Survey

- There is insufficient evidence of benefit to recommend routine follow up skeletal surveys in untreated asymptomatic patients in the absence of signs of disease progression.
- In the event of clinical or laboratory evidence of disease progression in treated or untreated patients, the skeletal survey should be repeated as part of the restaging process. Any newly symptomatic areas of the skeleton should be specifically targeted. However, if disease progression occurs within 3 months of the previous skeletal survey, in the absence of new skeletal symptoms, a new skeletal survey is unlikely to provide additional information (**Grade C recommendation; level IV evidence**).

MR Imaging

- There is insufficient evidence to recommend routine MR imaging for the follow up of treated disease.
- In selected cases, where there are persisting unexplained symptoms, it is reasonable to discuss the potential usefulness of follow up MR imaging with the radiologist (**Grade C recommendation; level IV evidence**).
- MR imaging is the investigation of choice for suspected avascular necrosis of the femoral head (**Grade B recommendation; level III evidence**).

Computed Tomography

- Routine follow up CT scanning of treated disease cannot be recommended on current evidence and concern regarding radiation exposure.
- In selected cases, however, it is reasonable to use CT scanning in the monitoring of the response of soft tissue masses to therapy (**Grade B recommendation; level III evidence**).
- In selected cases, where there are persistent unexplained symptoms or there is concern about on-going fracture risk, or a lack of response to therapy, it is reasonable to discuss the potential usefulness of performing a CT scan in treated patients (**Grade B recommendation; level III evidence**).

PET and MIBI Scanning

- Neither PET nor MIBI scanning can be recommended on the basis of current evidence for use in routine follow up of treated myeloma patients.
- It would be reasonable to consider either technique for the follow up of selected patients, such as those with predominant extramedullary or non-secretory disease, but this would be best performed in the context of a clinical trial (**Grade C recommendation; level IV evidence**).

Definitions:

Levels of Evidence

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Ib Evidence obtained from at least one randomised controlled trial

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Grade B, Evidence levels IIa, IIb, and III Recommendation based on well-conducted studies but no randomised controlled trials on the topic of recommendation

Grade C, Evidence level IV Evidence from expert committee reports and/or clinical experiences of respected authorities

CLINICAL ALGORITHM(S)

The original guideline document contains the clinical algorithm "Algorithm of Suggested Recommendations."

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is given for selected recommendations (see "Major Recommendations").

There is a distinct lack of randomised controlled trials in the use of imaging in myeloma, and the relationship between diagnostic imaging information and patient outcomes is difficult to demonstrate due to the multiple steps and confounding factors that intervene, including individual patient performance status, prognostic factors and treatment modalities undertaken. Thus all the

recommendations made are of Grade B (based on well conducted studies but not randomized controlled trials) or grade C (evidence from expert committee reports and/or clinical experiences of respected authorities).

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Appropriate use of imaging in the management of myeloma

POTENTIAL HARMS

- Excess radiation exposure
- Increased waiting times until treatment
- Wasted limited resources if imaging does not improve diagnosis or prognosis

CONTRAINDICATIONS

CONTRAINDICATIONS

Magnetic resonance imaging is contraindicated in patients with intraorbital metallic foreign bodies or cardiac pacemakers.

QUALIFYING STATEMENTS

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Detailed imaging technical protocols are not included; they are beyond the scope of the guideline document.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Safety

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

D'Sa S, Abildgaard N, Tighe J, Shaw P, Hall-Craggs M. Guidelines for the use of imaging in the management of myeloma. Br J Haematol 2007 Apr;137(1):49-63. [115 references] PubMed

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2007 Apr

GUIDELINE DEVELOPER(S)

British Committee for Standards in Haematology - Professional Association

SOURCE(S) OF FUNDING

British Committee for Standards in Haematology

GUIDELINE COMMITTEE

Not stated

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

GUIDELINE STATUS

This is the current release of the guideline.

GUIDELINE AVAILABILITY

Electronic copies: Available from the British Committee for Standards in Haematology Web site.

Print copies: Available from the British Committee for Standards in Haematology; Email: bcsh@b-s-h.org.uk.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

None available

NGC STATUS

This NGC summary was completed by ECRI Institute on March 17, 2008. The information was verified by the guideline developer on April 1, 2008.

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